

CLAIMS

1. A method for providing at least one selected sequence in a nucleic acid with interstrand cross-links comprising hybridising at least one selected single strand sequence with a complementary single strand nucleic acid or a functional  
5 analogue thereof, wherein said selected sequence or said complementary nucleic acid or both comprise a cross-linking agent.

2. A method according to claim 1, wherein said functional analogue of said complementary single strand nucleic acid  
10 comprises peptide nucleic acid.

3. A method according to claim 1 or claim 2, wherein said selected interstrand cross-links hamper further hybridisation and/or replication of said selected sequences.

4. A method for the generation of a probe wherein at least  
15 one selected sequence in said probe is at least in part prevented from functioning as a probe through providing said selected sequence with interstrand cross-links by a method according to anyone of claims 1-3.

5. A method according to claim 3 or claim 4 wherein at  
20 least one of said selected sequence comprises at least one repetitive sequence.

6. A method according to anyone of the claims 1-5 wherein the cross-linking agent comprises a transition metal, preferably platinum.

25 7. A method according to anyone of the claims 1-6 wherein the cross-linking agent is trans-dichlorodiammineplatinum(II).

8. A method for the selected amplification of certain amplifiable sequences from a pool of amplifiable sequences comprising producing a selected interstrand cross-linked  
30 nucleic acid or probe, obtainable by a method according to anyone of the claims 1-7, to decrease the amount of

amplification of a subset of amplifiable sequences and subjecting said pool to an amplification reaction.

9. A method according to claim 8 wherein a single stranded nucleic acid is prevented from taking part in said
- 5 amplification through disabling the primer extension function of said single stranded nucleic acid, preferably through modification of the 3'-hydroxy group.
10. A method according to claim 8 or claim 9, wherein said pool is selected from sequences present in a chromosome.
- 10 11. A collection of amplified sequences obtainable by a method according anyone of the claims 8-10.
12. A probe for the detection of nucleic acid comprising a collection of labelled amplified sequences according to claim 11.
- 15 13. A method referred to as COBRA for the labelling of a set of at least two bio-organic molecules with a set of at least two colours, comprising generating said set of colours through combining ratio labelling with binary labelling.
14. A method according to claim 13, wherein the total number
- 20 of distinguishable colours of said combination can, at least in the case wherein two fluorophores are simultaneously used per target, be calculated according to the formula I

$$I: \text{No. of colours} = (n + ((r \times n!) / (2 \times (n - 2)!))) \times 2^m$$

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wherein  $n$  is the number of fluorophores used for ratio labelling,  $m$  is the number of fluorophores used to binary label the same target, and  $r$  is the number of ratios that is resolved by ratio labelling.

- 30 with :  $2 \leq n \leq \infty$ ,  
 $0 \leq r \leq \infty$

$$0 \leq m \leq \infty$$

15. A method according to claim 13 or claim 14, wherein at least one of said bio-organic molecules comprises nucleic acid, protein, carbohydrate and/or lipid.
- 5 16. A method for simultaneous identification of sequences of at least one chromosome or part thereof, through the use of at least one probe according to claim 12, wherein said probe is labelled according to a COBRA method for doubling the number of identifiable labels obtainable by ratio labelling, 10 comprising adding to a first set of fluorophores, used for the ratio labelling of a first set of probes, a novel fluorophore and labelling a second set of probes.
17. The use of a probe according to claim 12 for the detection of chromosomes or parts thereof.
- 15 18. The use of selected interstrand cross-links for decreasing the amount of amplified product of certain amplifiable sequences.
19. The identification of a disease through the typing of at least one chromosome wherein at least one chromosome is 20 labelled, with at least one probe labelled according to anyone of the claims 13-15, or by a method according to claim 16 or a probe according to claim 12.
20. A kit for the detection of nucleic acid comprising at least one probe according to claim 12.
- 25 21. A kit for performing a method according to anyone of claims 13-16 comprising at least one probe labelled with a COBRA method.
22. A kit for generating a probe according to claim 12, comprising at least a cross-linking agent, preferably linked 30 to a single stranded nucleic acid.

23. A molecule comprising at least two parts, cross-linked with a cross-linking agent, wherein said cross-linking agent comprises a transition metal, preferably platinum, wherein at least two of said parts comprise a protein.